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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/475,972 12/29/99 CARIELUX

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EXAMINER

HM12/0214

CLEMENS, K.

ART UNIT

PAPER NUMBER

1644

7

DATE MAILED:

02/14/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/475,072

Applicant(s)

CADIEUX, ALAIN

Examiner

Karen Clemens

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2000.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 2-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☒ The proposed drawing correction filed on 30 December 1999 is: a) ☒ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

DETAILED ACTION

1. Applicant's amendment, filed 12/4/00 (Paper No. 6), is acknowledged.
2. Claims 2-26 are pending and under consideration.
3. The following are new grounds of rejection necessitated by the amendment filed 12/4/00 (Paper No. 6):

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

- A. Claims 2-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a method for the treatment of asthma, bronchospastic disease characterized by airway hyperreactivity, and lung inflammatory diseases characterized by increased eosinophilia wherein said method comprises the administration of an active agent selected from the group consisting of CGRP, adrenomedullin and [Cys(ACM)^{2,7}] CGRP. However Applicant has only disclosed a ^{mammalian} *mammalian Calcitonin Gene-Related Peptide, adrenomedullin and [Cys(ACM)^{2,7}] Calcitonin Gene-Related Peptide*. The term, "CGRP" is defined on page 17 (see lines 3-10, in particular) of the specification as any peptide from any species which shares significant structural and functional homology with the calcitonin gene-related peptide, i.e. functions as CGRP. The claims therefore reads on *any* peptide from *any* organism which shares significant structural and functional homology with the calcitonin gene-related peptide.

Consequently, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See *Regents of the University of California v. Eli Lilly & Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicant is also directed to the Guidelines for the Examination of Patent

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Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

B. Claims 2-26 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for the method of *treatment* of asthma, bronchospastic disease characterized by airway hyperreactivity, and lung inflammatory diseases characterized by increased eosinophilia wherein said method comprises the administration of an active agent selected from the group consisting of mammalian Calcitonin Gene-Related Peptide, adrenomedullin and [Cys(ACM)^{2,7}] Calcitonin Gene-Related Peptide does not reasonably provide enablement for the method of *prevention* or treatment of the pathophysiological manifestations of the aforementioned diseases for all CGRP peptides or [Cys(ACM)^{2,7}] CGRP.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the unpredictability in the art and amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims. The instant claims 22-26 are directed to a "method of *prevention* or treatment of the *pathophysiological manifestations of a disease*". The broadest reasonable interpretation of the claims is the *prevention* of the aforementioned pulmonary diseases since the *pathophysiological manifestations* are included in the criteria for diagnosis of the said diseases. It is assumed that applicant intends to permanently "prevent" asthma, bronchospastic diseases characterized by airway hyperreactivity, and lung inflammatory diseases characterized by increased eosinophilia via administration of CGRP. However, although Calcitonin Gene Related Peptide has been disclosed in the specification to *reduce the intensity* of the bronchospasms induced by an asthmatic crisis and to act as an anti-inflammatory agent in the lung (see specification, page 7-9, summary of the invention in particular) the actual *prevention* of the pulmonary diseases would require immunological tolerance to the proposed allergen eliciting the inflammatory response prior to the onset of the disease (see Merck Manual, pages 556-568, of record).

In addition, the term, "CGRP" is defined on page 17 (see lines 3-10, in particular) of the specification as any peptide from any species which shares significant structural and functional homology with the calcitonin

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gene-related peptide, i.e. functions as CGRP. Consequently the claim reads on *any* peptide from *any* organism which shares significant structural and functional homology with the calcitonin gene-related peptide. The specification provides insufficient guidance on the use of such homologs, analogs, fragments or derivatives of CGRP other than *mammalian Calcitonin Gene Related Peptide, adrenomedullin, and the linear analog, [Cys(ACM)^{2,7}] Calcitonin Gene Related Peptide* for the *treatment* of the aforementioned diseases. The specification disclosure is silent with respect to the specific features necessary for such "CGRP" homologs, analogs, fragments and derivatives such that they can be used successfully in the method of treating the aforementioned diseases.

In addition, the current state of the art for protein structure/function prediction based on primary amino acid sequence data is currently inadequate given the multifunctional nature of proteins (see Skolnick et al.). Furthermore, It is not routine in the art to screen large numbers of homologs, analogs, fragments and derivatives of CGRP to determine which peptides would possess the functional criteria based on the instant disclosure. A skilled artisan would require guidance, such as information regarding the amino acid sequences of the homologs, analogs, fragments or derivatives of "CGRP" required to preserve the biological, structural or functional features of the protein in order to make and use the molecules in a manner reasonably commensurate with the scope of the claims. Therefore, it would take an undue amount of experimentation for one skilled in the art to determine which homologs, analogs, fragments and derivatives of "CGRP" are encompassed by the instant claims.

In view of the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take an undue amount of experimentation for one skilled in the art to practice the full scope of the claimed invention.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent."

Claims 2-26 are rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 5,858,978 as evidenced by the Merck Manual (see pages 556-557) for the same reasons set forth in Paper No. 5, dated 8/2/00.

Applicant's arguments, filed 12/4/00 (Paper No. 6), have been fully considered but are not found persuasive.

Applicant submits that the '978 Patent is not enabling with regard to the use of Calcitonin Gene Related Peptide for the treatment of asthma and other airway disorders since the '978 Patent teaches that the Calcitonin Gene Related Peptide mechanism of action involves the inhibition of IL-1 (and indirectly, IL-2) released from macrophages and giant cells. Applicant submits that this cannot be extrapolated to the treatment or regulation of any condition involving inflammation, such as asthma, given the pleiotropic nature of cytokine activity, and the enormous variation and complexity of the mediating factors and regulatory systems involved in the manifestation of such disorders.

However the Examiner notes that issued Patents are considered enabled upon issue and are relevant as prior art for all they contain (see MPEP 2123). Further the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known. Even though Applicant's mechanism of action differs from the '978 Patent it does not distinguish the prior art teaching the same methods to achieve the same end result (see MPEP 2145). Moreover, the state of the art at the time of the invention recognized that IL-1 *does* have a role in allergic disease. IL-1 participates in the inflammation associated with asthma, is generated in asthmatic airways and generates some degree of bronchoconstriction (see Rosenwasser, page 348, column 2 in particular). In addition, Rosenwasser further notes that the IL-1 receptor antagonist *inhibits* antigen induced pulmonary eosinophil accumulation in airway hyperreactivity.

5. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made."

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Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person subject to an obligation of assignment to the same person.

Claims 2-26 are rejected under 35 U.S.C. §103(a) as being unpatentable over Vignery (U.S. Patent No. 5,858,978) in view of Gleich et al. (U.S. Patent No. 5,510,339) for the same reasons set forth in Paper No. 5, dated 8/2/00.

Applicant's arguments, filed 12/4/00 (Paper No. 6), have been fully considered but are not found persuasive.

Applicant argues that the '978 Patent fails to teach the link between the ability of Calcitonin Gene Related Peptide to inhibit IL-1 release and asthma and that, as this link is believed to be weak, the second reference, the '339 Patent, which is focussed on asthma and its association with increased eosinophilia was sought based on hindsight using information derived from the instant application.

However, as noted above, the '978 Patent is considered enabled as the cytokine, IL-1, was known in the art to be linked with asthma, thereby supporting the use of the '339 Patent as a secondary reference.

In addition, in the U.S.C. §102 rejection in the Office Action dated 8/2/00, the Merck Manual was also used as evidence to emphasize that asthma is well known in the art as a bronchospastic disease characterized by airway hyperreactivity and lung inflammatory reaction with an increase in eosinophils (see Merck Manual, pages 556-557 in particular).

Applicant is invited to submit the Declaration mentioned in the amendment filed 12/4/00 to provide evidence that the Applicant's invention was realized prior to the filing date of U.S. Patent No. 5,858,978 (which is a Continuation of application Serial No. 08/125,275, filed 9/23/93, which is a Continuation of application Serial No. 07/408,573, filed 9/18/89).

6. No claim is allowed.


Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Clemens whose telephone number is (703) 308-8365. The examiner can normally be reached Monday through Friday from 8:00 AM to 5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Karen Clemens, Ph.D.
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Technology Center 1600
February 9, 2001


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